

Award Number: W81XWH-09-2-0065

TITLE: Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness

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CONTRACTING ORGANIZATION: East Carolina University
Greenville, NC 27834

REPORT DATE: July 201H

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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| REPORT DOCUMENTATION PAGE | | | Form Approved
OMB No. 0704-0188 | | |
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| 1. REPORT DATE
July 201H | | 2. REPORT TYPE
Annual | | 3. DATES COVERED
1 July 201G– 30 June 201H | |
| 4. TITLE AND SUBTITLE

Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness | | | | 5a. CONTRACT NUMBER | |
| | | | | 5b. GRANT NUMBER
W81XWH-09-2-0065 | |
| | | | | 5c. PROGRAM ELEMENT NUMBER | |
| 6. AUTHOR(S)

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E-Mail: { ^**•, O^&~ Èâˆ | | | | 5d. PROJECT NUMBER | |
| | | | | 5e. TASK NUMBER | |
| | | | | 5f. WORK UNIT NUMBER | |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

East Carolina University
Greenville, NC 27834 | | | | 8. PERFORMING ORGANIZATION REPORT
NUMBER | |
| 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012 | | | | 10. SPONSOR/MONITOR'S ACRONYM(S) | |
| | | | | 11. SPONSOR/MONITOR'S REPORT
NUMBER(S) | |
| 12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited | | | | | |
| 13. SUPPLEMENTARY NOTES | | | | | |
| 14. ABSTRACT

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OF ABSTRACT | 18. NUMBER
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USAMRMC |
| a. REPORT
U | b. ABSTRACT
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Table of Contents

| | <u>Page</u> |
|-----------------------------------|-------------|
| Introduction..... | 5 |
| Body..... | 6 |
| Key Research Accomplishments..... | 7 |
| Reportable Outcomes..... | 7 |
| Conclusion..... | 7 |
| References..... | 7 |
| Appendices..... | 7 |

INTRODUCTION

Gulf war veterans' illnesses comprise distinct clusters of symptom-defined illnesses (1,2) for which there are neither diagnostic tests nor effective treatments. Gulf war veterans had variable exposures to a number of chemicals (3), including organophosphate insecticides, pyrethrum-related insecticides, DEET, Pyridostimine bromide, smoke from oil well fires, and Sarin gas. Gulf war veterans' illnesses may reflect an inflammatory cycle involving the brain which may be a common mechanism of many neurological conditions, whether initiated by toxic exposures, infection, or trauma. In this theory, central nervous system inflammation initiated by toxic exposures and sometimes exacerbated by subsequent exposures is a component of illness hypothesized to explain the neurological manifestations. Substance P release at sensory nerve endings is an explanation for the peripheral pain manifestations of illness.

This theory suggests that novel anti-inflammatory drugs may be of benefit in symptom-defined illnesses related to a cycle of inflammation. Dr. J. S. Hong's laboratory at the National Institute of Environmental Health Sciences has demonstrated that Morphine-related analogs, including Naltrexone and Dextromethorphan, have great potency in anti-inflammation and neuroprotective effects. Naltrexone is a safe and readily available generic medication. Dextromethorphan is also a safe and readily available generic medication that is available without a prescription as a cough medication. Results from several clinical trials showed that Naltrexone is effective in several inflammation-related diseases, such as neurogenic pain, movement disorders, etc. In addition, there were no obvious side effects in patients taking this drug for six months. This project is a randomized double-blinded studies for treating ill Gulf war veterans with Naltrexone and Dextromethorphan. Laboratory tests for markers of inflammation including neurogenic inflammation will be performed pre- and post-treatment, to see if these markers are elevated and if so, to see if treatment modulates these markers.

BODY

The major accomplishment of the past year was successfully recruiting and enrolling veterans with Gulf War Illness in the study. Compliance of those enrolled has been excellent.

A no cost extension has been obtained, so we can continued the study for a final year. We anticipate accomplishing study goals and objectives.

KEY RESEARCH ACCOMPLISHMENTS

The most significant accomplishment during the past year was successfully recruiting and enrolling significant numbers of veterans with Gulf War Illness in the clinical trials. Compliance with study protocols has been excellent. Data collection has been complete with no gaps on last data review.

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| Total Enrolled | 41 |
| Loss to follow-up | 1 |
| Completed combined naltrexone & dextromethorphan protocol | 2 |
| Completed naltrexone only protocol | 1 |
| Completed dextromethorphan only protocol | 1 |
| Currently enrolled in naltrexone protocol | 27 |
| Currently enrolled in dextromethorphan protocol | 27 |
| Discontinued naltrexone due to adverse reaction (subjective dizziness) | 1 |
| Discontinued dextromethorphan due to adverse reaction | 0 |

In addition, we successfully obtained a no cost extension to continue the study for the coming year. We anticipate a successful outcome to the study at the end of this annual study period.

Our goal is to meet the study target of 60 patients enrolled. We have stepped up recruitment efforts.

REPORTABLE OUTCOMES

No data has been analyzed. There has been only one adverse event, with one subject reporting subjective dizziness while taking naltrexone. This was discontinued and he proceeded to the dextromethorphan arm.

CONCLUSIONS

Successful recruitment, enrollment, compliance, and data collection has been gratifying. We anticipate a successful outcome to the study aims and objectives.

REFERENCES

1. Haley RW, Hom J. Is there a Gulf War Syndrome? Searching for syndromes by factor analysis of symptoms. JAMA. 1997;277:215-22. Erratum in: JAMA 1997 Aug 6;278(5):388.
2. Haley RW, Hom J, Roland PS, Bryan WW, Van Ness PC, Bonte FJ, Devous MD Sr, Mathews D, Fleckenstein JL, Wians FH Jr, Wolfe GI, Kurt TL. Evaluation of neurologic function in Gulf War veterans. A blinded case-control study. JAMA. 1997;277:223-30.
3. Haley RW, Kurt TL. Self-reported exposure to neurotoxic chemical combinations in the Gulf War. A cross-sectional epidemiologic study. JAMA. 1997;15;277:231-7.